Evaluation of Parotid Gland Function Before and After Endoscopy-Assisted Stone Removal

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Purpose: To quantify gland function before and after endoscopy-assisted lithectomy for patients with parotid stones and to analyze correlations among different evaluation modalities.

Materials and Methods: This study investigated 58 patients (27 men and 31 women) with a stone larger than 5 mm or multiple parotid stones who underwent successful endoscopy-assisted surgery at the authors' center from August 2007 through September 2017. Meticulous postoperative manipulations were administered routinely for 3 to 6 months to promote functional recovery of the affected gland. Gland function was evaluated preoperatively and 6 to 36 months (mean, 12 months) postoperatively by sialography, scintigraphy, and sialometry. Statistical analyses were conducted to quantify gland function recovery and to distinguish correlations among the 3 objective tests.

Results: Preoperative sialograms exhibited ductal ectasia at the stone site with ductal stenosis anterior to the stone (n = 53) or duct interruption at the stone site (n = 5). Postoperative sialograms of 45 patients without stones were categorized as approximately normal (type I; n = 17); showing ectasia or stenosis of the main duct without persistent contrast on the functional film (type II; n = 16); showing ectasia or stenosis of the main duct with mild contrast retention (type III; n = 6); or showing poor ductal shape with evident contrast retention (type IV; n = 6). Scintigraphy of 23 preoperative and 12 postoperative patients and sialometry of 24 preoperative and 12 postoperative patients indicated severe preoperative impairment and postoperative improvement of gland function. Postoperatively, although no relevant differences in saliva flow rate were found between the 2 sides, scintigraphy showed lower function of the affected gland compared with the control side. Statistical data showed positive correlations among the 3 methods. Sialography intuitively reflected the ductal shape, whereas sialometry and scintigraphy were more sensitive for evaluating gland function.

Conclusion: For patients with parotid stones, minimally invasive endoscopic surgery and meticulous postoperative manipulations help preserve the glands and facilitate recovery of gland function. The 3 evaluating modalities have certain positive correlations.

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Sialolithiasis is one of the most common non-neoplastic diseases of the major salivary glands and occurs in approximately 0.45 to 1.20% of the general population.[1] Sialoliths affect the parotid gland in approximately 10 to 20%.[2] Since the development of sialendoscopy, most parotid gland calculi can be successfully removed with preservation of the gland.[3-6] The reported success rates range from 80 to 94.8%, with a low rate of complications.[6] However, middle- to long-term follow-up of the function of the involved gland is based mainly on the subjective evaluation of symptoms and signs.[7] Because of preoperative impairment and intraoperative injury of the ductal system and parenchyma, postoperative recovery of gland function varies greatly. An objective and accurate evaluation of gland function might help optimize intra- and postoperative manipulations.

Objective evaluation methods of salivary gland function mainly include sialography, scintigraphy, and sialometry,[6-12] which are scarcely reported for parotid stone cases.[6,12] Sialography is a qualitative tool that depicts the shape of the ductal system and evacuation of contrast medium, representing gland function.[8,9] Scintigraphy and sialometry are quantitative methods for the assessment of gland function.[10-12] Nevertheless, these 3 objective methods have their limitations and their combined use is often needed. To date, no studies have evaluated pre- and postoperative parotid gland function by the combined use of these 3 methods.[12-14] The aim of the present study was to evaluate pre- and postoperative gland function by these 3 methods and to distinguish the probable correlations among them.

Materials and Methods

PATIENTS

From August 2007 through September 2017, 188 patients with parotid gland calculi underwent endoscopy-assisted lithectomy at the authors' center. For a proportion of patients, pre- and postoperative gland function evaluations were performed by sialography, sialometry, or scintigraphy or their combination.

Inclusion criteria for the study sample were *1)* patients 20 to 75 years old, *2)* successful removal of the calculi, and *3)* a stone larger than 5 mm or multiple stones. Exclusion criteria were *1)* patients with acute infection of the parotid gland or those with severe illness who could not tolerate any operative procedures, *2)* gland removal or ligation of the main duct during the operation, and *3)* severe stricture of the main duct.

The study design was approved by the institutional review board of the authors' institution (PKUSSIRB-201412005), and all participants signed an informed consent.

Fifty-eight patients were recruited for this study (27 men and 31 women; age range, 22 to 75 yr; mean age, 47 yr). Fifty had a single stone (6 to 10 mm; mean, 7 mm) and 8 had multiple stones. All patients underwent preoperative sialography. In addition, 22 patients underwent sialometry and scintigraphy, 2 underwent sialometry, and 1 underwent scintigraphy. Calculi were successfully removed through a transoral approach in 42 cases (Figs 1, 2), through a buccal incision in 10 (Fig 3), and through a preauricular flap in 6 (Fig 4). After success of the initial surgery, daily massage of the involved gland after stimulation with sialagogues was recommended. Terminal duct dilation and intraductal administration of saline and cortisone were performed once a month for 3 to 6 months. For patients with evident symptoms, follow-up endoscopy was performed. At 6 to 36 months postoperatively (mean, 12 months), 45 patients returned to the clinic and underwent sialography. Of these 45 patients, 5 underwent scintigraphy, 5 underwent sialometry, and 7 underwent sialometry and scintigraphy. The

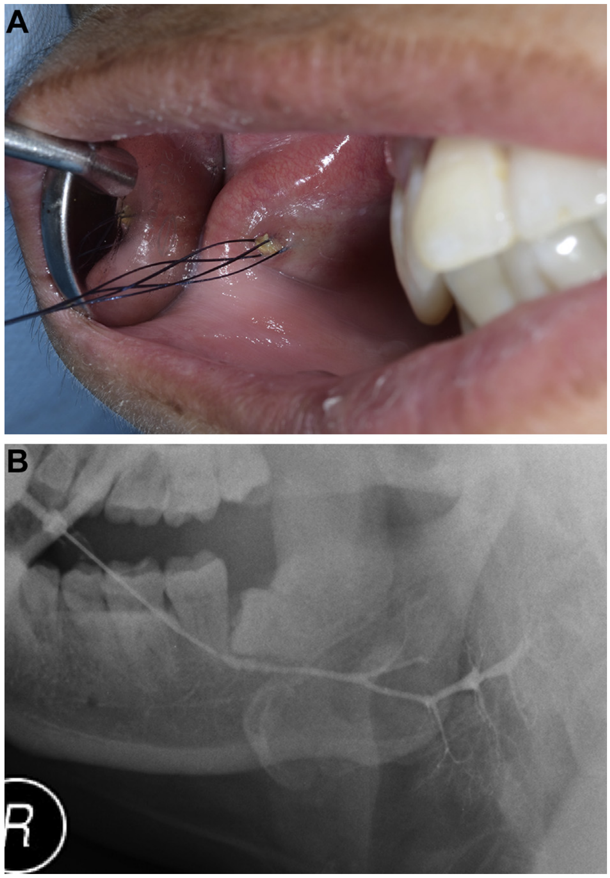

FIGURE 1. A right parotid stone removed by direct basket retrieval. *A,* The stone was entrapped by the basket and pulled to the ostium. The patient remained asymptomatic 6 months after the operation. *B,* Follow-up sialogram displayed an approximately normal shape of the main duct.

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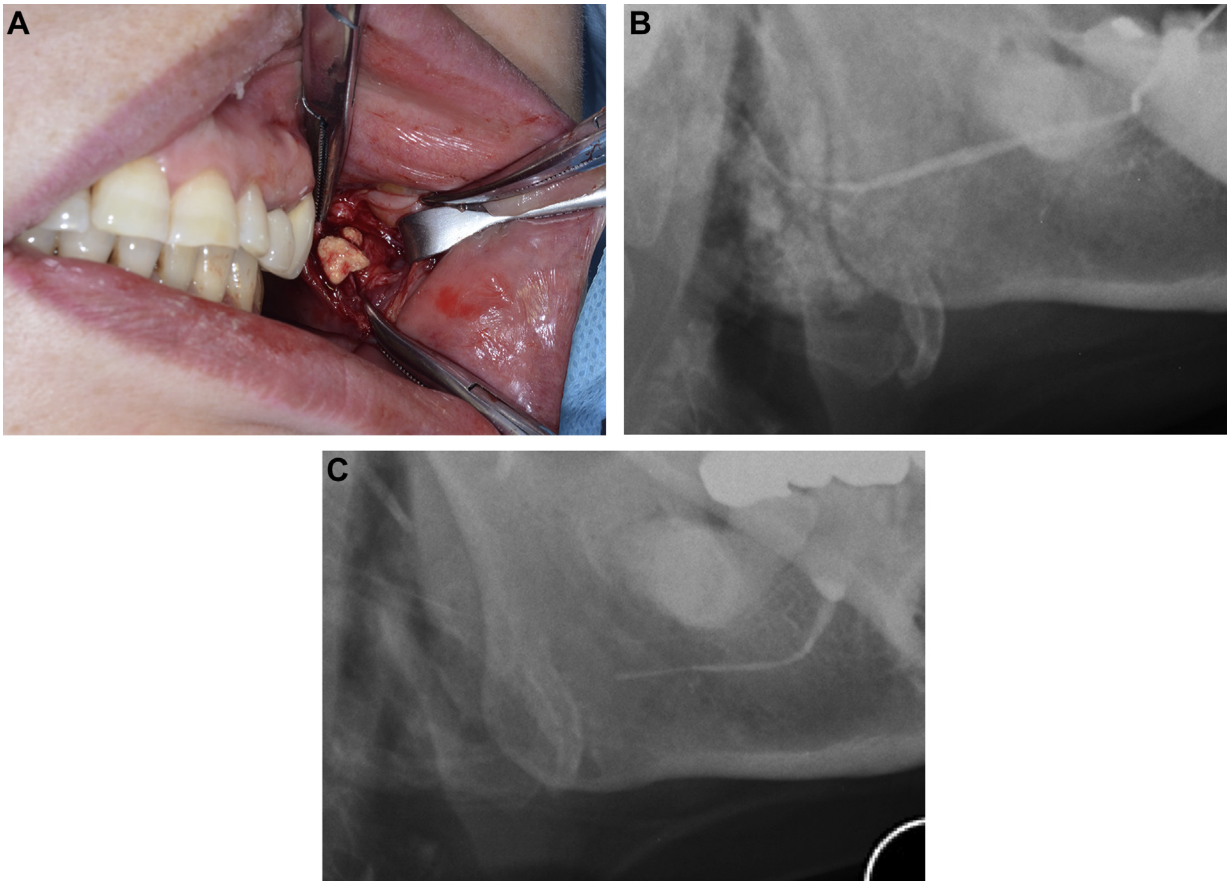

FIGURE 2. An impacted stone at the anterior third of the left Stensen duct removed transorally. *A*, The stone was exposed through a parosteal incision. The patient remained asymptomatic 9 months after the operation. Follow-up sialograms showed ectasia of the main duct on the *B*, filling film with mild contrast retention on the *C*, functional film.

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remaining 13 patients who did not return to the clinic reported they were asymptomatic during telephone inquiries.

METHODS EVALUATING GLAND FUNCTION

Sialography

After introduction of the catheter, 1.5 to 2 mL of contrast was carefully infused. Subsequently, a lateral view and a 5-minute emptying film were recorded. Appearance of the ductal system and gland function were analyzed. Each film was independently analyzed by 2 experienced oral and maxillofacial radiologists who reached a consensus by discussion. Sialograms were divided into 4 types: approximately normal (type I; Fig 1B); the main duct had ectasia or stenosis (Fig 3D) but no persistent contrast was seen on functional films (type II); the main duct had ectasia or stenosis with mild contrast retention on functional films (type III; Fig 2B, C); or the main duct had ectasia or stenosis and contrast retention was evident on functional films (type IV; Fig 4B, C). For gland function, types I and II were scored as fair and types III and IV were scored as poor.

Scintigraphy

Single-photon emission tomography (Discovery NM/CT 670; GE Medicine Systems, Dhaka, Bangladesh) was used for image collection. The device had a dual-head and a shooting time of 30 minutes and an image was collected every 60 seconds. The matrix was 64 × 64. After intravenous injection of sodium technetium-99m (99mTc) and pertechnetate 5 mCi, dynamic images of blood flow were collected. Stimulation with vitamin C 100 mg on the dorsal side of the tongue was performed 20 minutes later. Regions of interest (ROIs) were drawn manually on dynamic images of the bilateral parotid by a professional nuclear medicine physician. The background ROI was marked in the forehead region. Time-and-activity curves were generated for bilateral parotid glands. Based on these ROI counts and time-and-activity curves, the following functional values were defined for bilateral parotid glands: background value (B), maximum value of the parotid gland (Cmax), value of the parotid gland at 20 minutes (Cs), and minimum value after stimulation (Cmin). Thereafter, the following indices were calculated:

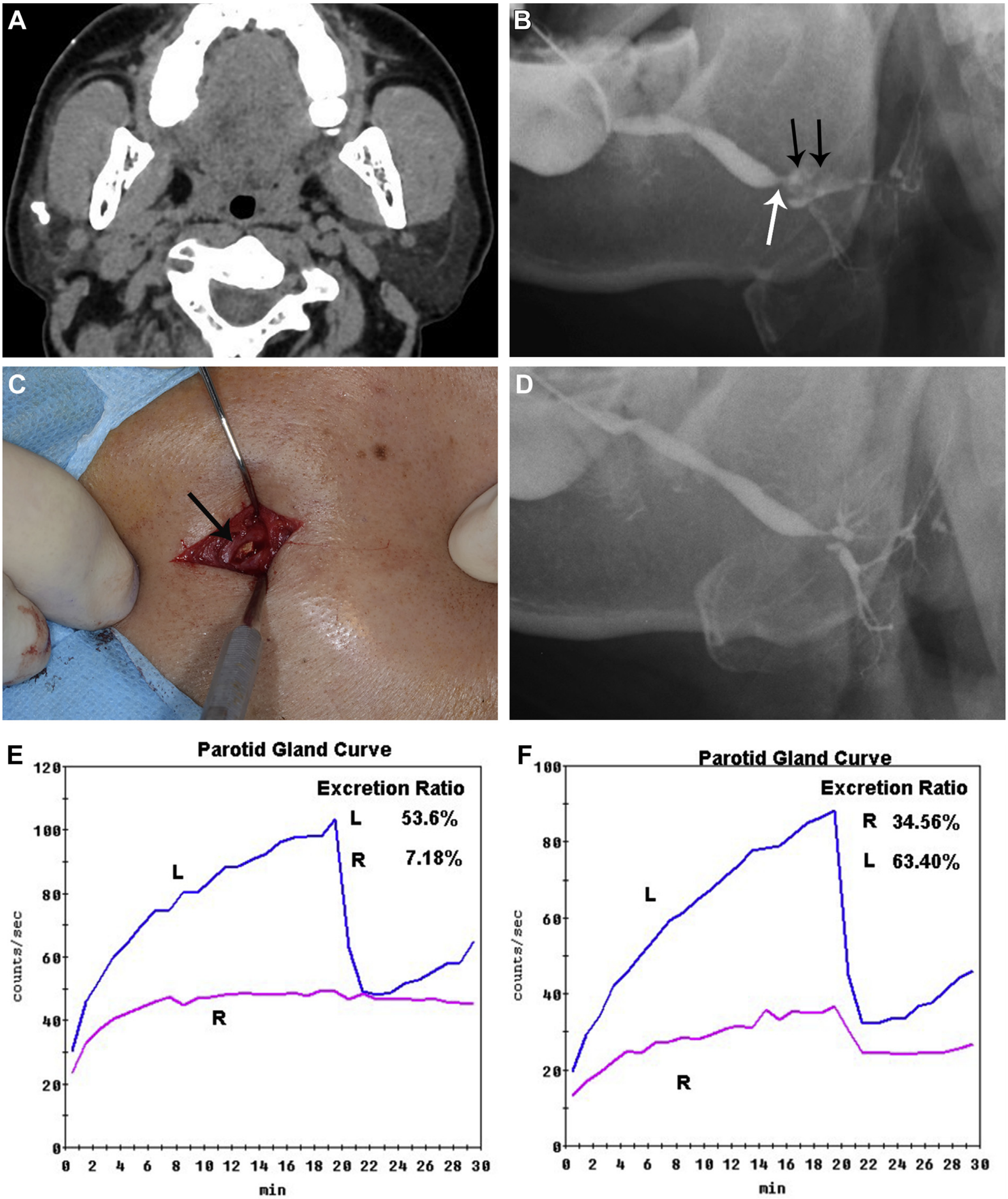

FIGURE 3. A hilum stone of the right parotid gland removed through a buccal incision. *A,* Axial computed tomogram displayed a hilum calculus of the right parotid gland. *B,* Preoperative sialogram showed stenosis (*white arrow*) of the main duct anterior to the stone, and the stone appeared as a filling defect (*black arrows*). *C,* The stone (*yellow arrow*) was removed through a minimal buccal incision. Note that the duct (*black arrow*) was sliced and the stone was exposed. The patient remained asymptomatic 18 months after the operation. *D,* Follow-up sialograms showed ectasia and stenosis of the main duct, without persistent contrast retention on the emptying film. *E,* Preoperative scintigraphy showed poor uptake and excretion of technhetium-99 in the right parotid gland. *F,* Postoperative scintigraphy showed improved technetium-99m excretion of the right parotid gland but still much lower than of the left side. Abbreviations: L, left; R, right.

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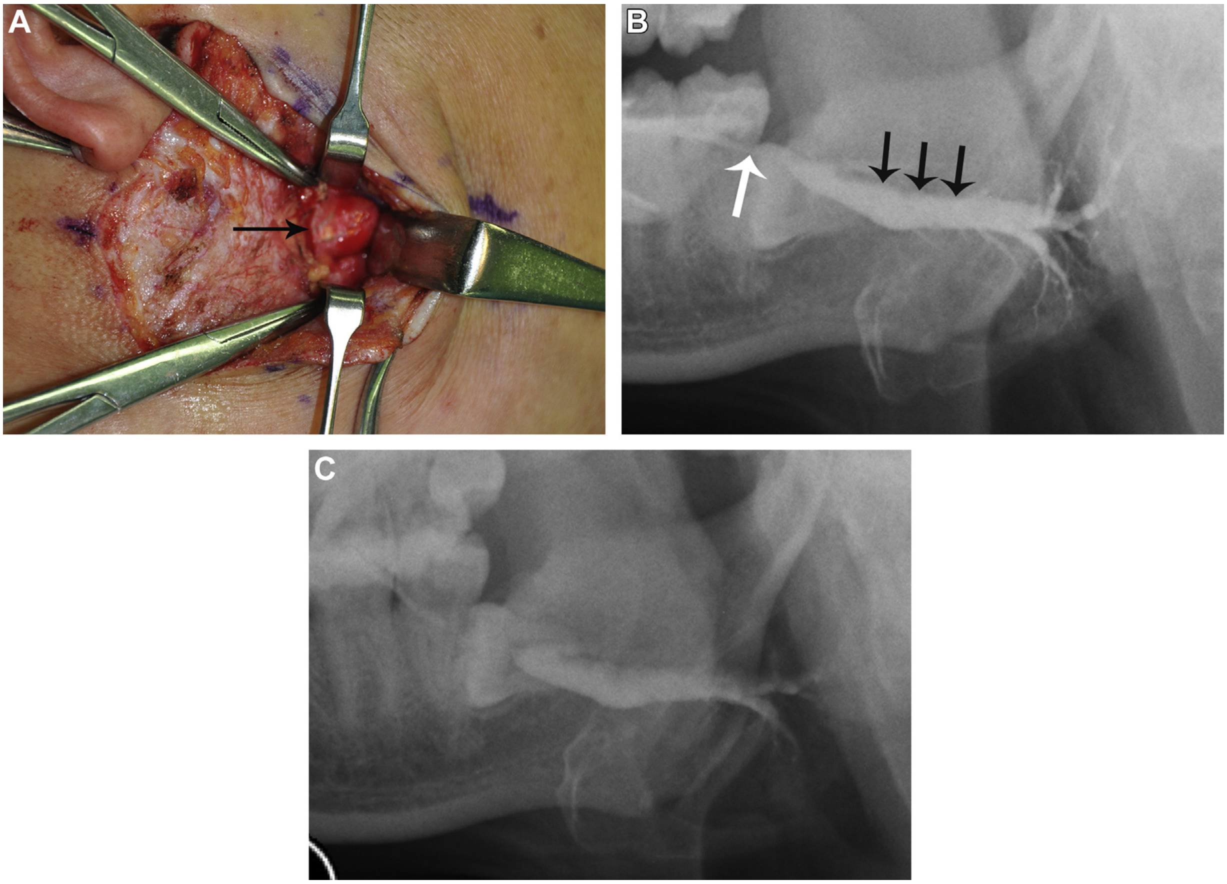

FIGURE 4. A hilum stone of the right parotid gland removed through a preauricular flap. *A,* The entrapped stone at the hilum of the main duct (*arrow*) was exposed through a preauricular flap. The patient had mild symptoms 6 months after the operation. Follow-up sialograms showed ectasia (*black arrows*) and stenosis (*white arrow*) of the main duct on the *B,* filling film with evident contrast retention on the *C,* functional film.

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$$\text{Concentration index(CI)} = (\text{Cmax} - \text{B})/\text{B}$$

$$\text{Secretion index(SI)} = (\text{Cs} - \text{Cmin})/(\text{Cs} - \text{B})$$

$$\text{Concentration index ratio(CIR)} = \text{CI}_{\text{affected}}/\text{CI}_{\text{unaffected}}$$

$$\text{Secretion index ratio(SIR)} = \text{SI}_{\text{affected}}/\text{SI}_{\text{unaffected}}$$

$$\text{Function index(FI)} = \text{CIR} \times \text{SIR}$$

Sialometry

Salivary flow rate was calculated at 9 to 11 AM by 2 researchers who were well calibrated. Before saliva collection, water and alcohol consumption and smoking were prohibited for at least 1 hour, and patients rinsed their mouths twice with clean water. Parotid saliva was collected by a modified Lushley cup, which was connected to a saliva storage device. The resting and stimulated salivary flow rates were each measured for 5 minutes. After saliva collection, saliva weight was measured by an analytical balance with a precision of 0.1 mg. The total saliva flow in 10 minutes was calculated by adding the resting saliva flow and the stimulated saliva flow. Then, the saliva secretion ratio (SSR) of the affected gland was calculated:

$$\text{SSR} = (\text{10-minute total flow of affected gland})/(\text{10-minute total flow of control gland})$$

STATISTICAL ANALYSIS

Statistical analyses were conducted using SPSS 22.0 (SPSS Inc, Chicago, IL). The quantitative parameters were expressed as mean $\pm$ standard deviation and Student t test was used to compare differences between the affected and unaffected control glands and between pre- and postoperative values if the data coincided with the Gaussian distribution; otherwise, the range and median of the values were provided and Wilcoxon rank sum test was used for comparison. The χ^2 tests were used to investigate the consistency between sialography and scintigraphy and between sialography and sialometry. Correlations between scintigraphy and sialometry were assessed by Spearman ρ analysis. Differences were considered significant for a P value less than .05.

Results

SIALOGRAPHY

In 5 of the 58 patients with preoperative sialograms, the main duct was interrupted at the stone site without filling of the proximal duct. In the other 53, ductal dilatation at the stone site and ductal stenosis anterior to the stone were seen (Fig 3B); stones exhibited a filling defect (n = 50) or a calcified mass (n = 3) and contrast retention were evident on the emptying film. Of the 45 patients with postoperative sialograms, 37 were asymptomatic and 8 had mild symptoms that could be relieved by self-massaging. Sialograms were scored as type I in 17 cases, type II in 16, type III in 6, and type IV in 6. In all 8 symptomatic cases, sialograms exhibited ductal strictures (type III in 3 cases and type IV in 5 cases). Detailed results are presented in Table 1. For gland function, type I and II sialograms of 33 patients were scored as fair and type III and IV sialograms of the other 12 patients were scored as poor.

SCINTIGRAPHY

Twenty-three patients underwent preoperative scintigraphy and 12 patients underwent postoperative scintigraphy (Fig 3E, F). Preoperatively, Wilcoxon rank sum test showed that the CI (0.00 to 2.70; median, 0.70) and SI (0.00 to 0.81; median, 0.00) of the affected gland were lower than the CI (1.10 to 3.65; median, 2.30) and SI (0.38 to 0.96; median, 0.77) of the contralateral gland (Z = 4.092, P = .000; Z = −4.170, P = .000). Postoperatively, paired t test showed that the CI (1.49 ± 0.67) and SI (0.39 ± 0.31) of the affected side were lower than the CI (2.46 ± 0.94) and SI (0.73 ± 0.16) of the unaffected side (t = 2.894, P = .015; t = 3.959, P = .002). In addition, Wilcoxon rank sum test showed that the postoperative CI (Z = 2.153, P = .031), SI (Z = 3.672, P = .000), and FI (Z = −3.270, P = .001) were higher than the preoperative values.

Table 1. POSTOPERATIVE SIALOGRAPHIC AND CLINICAL MANIFESTATIONS OF 45 PATIENTS

	Type I	Type II	Type III	Type IV	Total
Symptomatic	0	0	3	5	8
Stenosis	0	7	3	5	15
Dilatation	0	10	6	5	21
Total	17	16	6	6	45

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SIALOMETRY

Twenty-four patients underwent preoperative sialometry and 12 patients underwent postoperative sialometry. Wilcoxon rank sum test showed that the preoperative 10-minute saliva flow of the affected gland (0.00 to 0.49 g; median, 0.06 g) was significantly lower than that of the control side (0.26 to 3.82 g; median, 0.77 g; Z = −4.257, P = .000); however, no significant differences were found for the postoperative values between the affected gland (0.08 to 2.25 g; median, 0.56 g) and the control gland (0.17 to 5.12 g; median, 0.76 g; Z = −1.726, P = .084). Moreover, the postoperative SSR of the affected gland (0.01 to 1.65; mean, 0.49) was significantly higher than the preoperative SSR (0.01 to 1.10; median, 0.07; Z = 4.413, P = .000).

CORRELATIONS AMONG 3 OBJECTIVE TESTS

Correlation of Sialography and Scintigraphy

Twelve patients underwent postoperative sialography and scintigraphy; the sialograms were scored as fair in 9 cases and poor in 3. The FI was used as an indicator of scintigraphy, and 0.25 (0.5 × 0.5) was used as a dividing point. In 5 cases with an FI of at least 0.25, gland function was scored as fair; in the remaining 7 cases with an FI lower than 0.25, gland function was scored as poor. The χ^2 test showed no significant differences between sialography and scintigraphy for evaluating gland function (P = .125). Specifically, the function evaluations of sialography were consistent with those of scintigraphy in 8 patients. In the remaining 4 patients, sialograms were scored as fair, whereas scintigraphy showed poor function (Table 2).

Correlation of Sialography and Sialometry

Twelve patients underwent sialography and sialometry after surgery. Sialographic scores were fair for 10 patients and poor for 2 patients. For convenience of comparison, the SSR was used as an indicator of sialometry and 0.5 was used as a dividing point. In 6 cases with an SSR of at least 0.5, gland function was scored as fair; in the remaining 6 cases with an SSR less than 0.5, gland function was scored as poor. The χ^2 test showed no significant differences between sialography and sialometry for evaluating gland function (P = .125). Specifically, the function evaluations of sialography were consistent with those of sialometry in 8 patients. In the remaining 4 patients, sialograms were scored as fair, whereas sialometry showed poor function (Table 3).

Table 2. CORRELATION OF POSTOPERATIVE SIALOGRAPHY AND SCINTIGRAPHY IN 12 PATIENTS

Patient Number	Stone Size (mm) or Multiple Stones	Sialography Type	Sialographic Score	Function Index	Scintigraphic Score
1	7	I	Fair	0.61	Fair
2	10	I	Fair	0.49	Fair
3	6	II	Fair	1.07	Fair
4	Multiple stones	II	Fair	0.00	Poor
5	Multiple stones	II	Fair	0.22	Poor
6	Multiple stones	II	Fair	0.10	Poor
7	Multiple stones	III	Poor	0.00	Poor
8	10	III	Poor	0.00	Poor
9	6	I	Fair	1.31	Fair
10	7	I	Fair	0.14	Poor
11	6	II	Fair	0.44	Fair
12	10	IV	Poor	0.00	Poor

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Correlation of Scintigraphy and Sialometry

Twenty-two patients underwent scintigraphy and sialometry preoperatively and 7 patients underwent scintigraphy and sialometry postoperatively, including 3 patients who underwent postoperative scintigraphy and sialometry twice. Spearman ρ analysis showed that the preoperative FI (0.00 to 1.19; median, 0.00) was not correlated with the SSR (0.00 to 1.10; median, 0.07; $P = .891$). However, the postoperative FI had a positive correlation with the SSR ($r = 0.64$; $P = .044$; Fig 5).

Discussion

Since Katz[15,16] first introduced endoscopic techniques for the salivary glands, Nahlieli et al,[17] Karavidas et al,[18] McGurk et al,[19] Marchal,[20] Koch et al,[7] and Foletti et al[21] successively reported on their researches of endoscopy-assisted lithectomy for parotid stones. Pre- and postoperative evaluation of the parotid gland function was based mainly on clinical symptoms and signs. Moreover, objective function evaluation by sialography, scintigraphy, or sialometry was occasionally reported.[7,17-21]

Preoperative sialography is routinely contraindicated for parotid calculus cases for fear of proximal movement of mobile stones.[22] However, it can be used to estimate the ductal shape for impacted large stones (>5 mm).[6,17] In cases with distal duct ectasia and proximal duct stricture, the stones can be removed with relative ease. Conversely, distal duct stricture and proximal duct ectasia obviate endoscopic inspection and complicate stone removal. In the present study, most preoperative sialograms showed ductal stenosis anterior to the stone. According to Harrison,[23] stricture promotes saliva deposition and leads to the stagnation of

Table 3. CORRELATION OF POSTOPERATIVE SIALOGRAPHY AND SIALOMETRY IN 12 PATIENTS

Patient Number	Stone Size (mm) or Multiple Stones	Sialography Type	Sialographic Score	Saliva Secretion Ratio	Sialometric Score
1	10	I	Fair	1.21	Fair
2	Multiple stones	II	Fair	0.01	Poor
3	Multiple stones	II	Fair	0.39	Poor
4	Multiple stones	II	Fair	0.75	Fair
5	6	I	Fair	0.54	Fair
6	7	I	Fair	0.09	Poor
7	6	II	Fair	0.44	Poor
8	10	IV	Poor	0.25	Poor
9	6	I	Fair	1.41	Fair
10	8	I	Fair	0.75	Fair
11	6	II	Fair	1.65	Fair
12	Multiple stones	III	Poor	0.23	Poor

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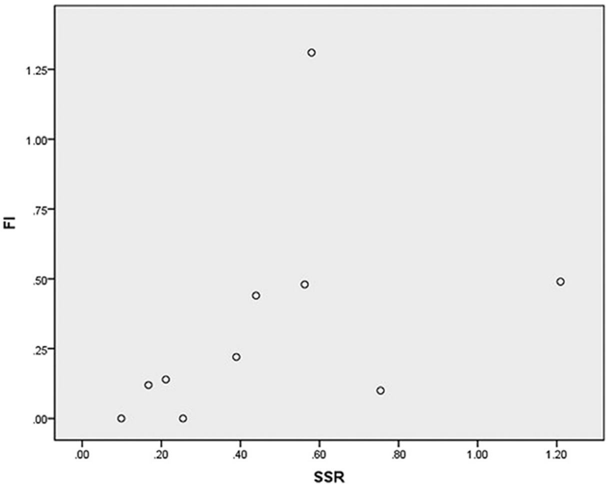

FIGURE 5. Postoperative scatterplot of the SSR and FI of the affected parotid gland. Abbreviations: FI, function index; SSR, saliva secretion ratio.

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secretory material rich in calcium, which is ideal for the formation of stones. After stone surgery, sialography can be used to evaluate ductal shape and gland function.[6,8] Forty-five postoperative sialograms were divided into 4 types. The 33 patients (73.3%) with type I or II sialograms were symptom free and can be evaluated as having good gland function. In the remaining 12 patients with type III and IV sialograms, 8 had mild discomfort, which can be correlated to ductal stenosis and poor contrast emptying on sialograms.[8]

Scintigraphy with 99mTc and pertechnetate is a safe and well-tolerated approach to evaluate salivary gland function and has been widely used in patients with various diseases.[12] The methodology of salivary scintigraphy differs across studies and there is no widely accepted standard value of normal salivary function.[24] In the present study, the FI was calculated to minimize bias. In 2004, Makdissi et al[25] used scintigraphy to assess pre- and postoperative gland function for 38 patients with hilum stones of the submandibular gland. The result showed improved function in 28 patients (52%), unchanged function in 5 patients (14%), and deterioration in 13 patients (34%). Moreover, the result showed that glandular recovery was inversely proportional to the size of the stone. Roh and Park[26] evaluated the efficacy of intraoral stone removal in patients with hilar submandibular stones by scintigraphy and found a marked postoperative improvement in 70% (38 of 54) of patients. Su et al[12] performed scintigraphy to analyze salivary gland function recovery after sialendoscopy in 17 patients, including 4 with parotid calculus. The result showed a marked preoperative decrease of uptake and excretion function and a marked postoperative increase in the affected glands. In the present study, the result showed notable postoperative improvement of gland function compared with preoperative values; however, the postoperative function of the affected glands was still considerably lower than that of the control side. Of the 7 patients with an FI lower than 0.25, 4 had multiple stones and 2 had 10-mm stones. Therefore, long-term follow-up, self-massage, and periodic intraductal infusion of saline and cortisone were recommended, especially for patients with larger or multiple stones.

Sialometric measurements include resting and stimulated saliva flow rates. Resting flow rate represents the baseline flow rate of salivary glands, and stimulated flow rate reflects the flow rate of salivary glands during chewing, tasting, or other stimulations. Salivary gland flow rate differs by gender, age, environment, patient's mental status, and measurement methods.[10,12] In the present study, amounts of resting and stimulated saliva were summed, and then the SSR between the affected and control glands was calculated. This calculation was first suggested to alleviate the bias caused by the aforementioned factors. The result showed a severe preoperative decrease and a marked postoperative improvement of the saliva flow rate. Of the 6 patients with an SSR lower than 0.5, 3 had multiple stones and 1 had a 10-mm stone. This confirmed that, even with severe inflammation, poor ductal shape, and intraoperative ductal slitting, postoperative gland function can be prominently improved. It should be stressed that dilatation of the ductal stricture, postoperative self-massage, and regular intraductal washing were helpful for this process.[23]

All 3 objective evaluation methods have disadvantages. Sialography and scintigraphy have a low dose of radiation. Further, sialography is contraindicated for patients who are allergic to contrast materials and has limitations in evaluating gland function because it is sometimes difficult to decide whether persistent contrast retention is caused by poor saliva secretion or by excessive infusion.[8,22] Scintigraphy machines are relatively expensive and seldom available in dental hospitals.[12] Also, sialometric analysis is deficient because of flow rate fluctuation under different situations.[10] In the present study, statistical results showed a positive correlation among sialography, scintigraphy and sialometry. In two thirds of patients, postoperative sialographic scores were consistent with those of scintigraphy and sialometry. In one third of cases, scintigraphy and sialometry showed worse results than sialography. This was certainly related to the dividing point set for the evaluation of gland function and indicated that sialometry and scintigraphy were more sensitive than sialography. Statistical analysis showed no correlations between preoperative scintigraphy and sialometry. This was probably because in most cases the duct was severely occluded and the FI was decreased to 0.00, which might affect the statistical results. Nevertheless, a positive correlation was found among their postoperative values. It can be speculated that, to some extent, scintigraphy and sialometry can be used interchangeably.

It should be stressed that only patients with larger or multiple stones were recruited for the present study, with the assumption that glandular recovery was inversely proportional to the size of the stone. Further, a proportion of patients were asymptomatic and reluctant to undergo these objective tests, so the follow-up ratio was not high. Moreover, each of the 3 evaluating methods has the aforementioned shortcomings, and no well-recognized evaluating criteria are found in the literature. All these might lead to a bias of statistical analysis and obviate further analysis among different surgical approaches or stone sites.

In summary, in patients with a stone larger than 5 mm or multiple parotid stones, preoperative sialograms showed ductal stenosis anterior to the stones in most cases, whereas more than 70% of postoperative sialograms showed improvement of ductal shape and gland function. Scintigraphy and sialometry indicated severe preoperative impairment and postoperative improvement of gland function. Postoperatively, although no relevant differences in saliva flow rate were found between the 2 sides, scintigraphy showed considerably lower function of the affected gland compared with the control side. The 3 objective examination results had certain correlations. Sialography intuitively reflected the morphology of the ductal system, whereas sialometry and scintigraphy were more sensitive for the determination of gland function.

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